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Effectiveness of Transdiagnostic Cognitive Behaviour Therapy for Anxiety and Depression in Adults: A Systematic Review and Meta-analysis

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Background: Transdiagnostic Cognitive Behaviour Therapy (CBT) seeks to identify core cognitive-behavioural processes hypothesized to be important across a range of disorders and to develop a treatment that targets these. This contrasts with standard CBT approaches that are disorder-specific. Proponents of transdiagnostic CBT suggest that it may offer advantages over disorder-specific CBT, but little is known about the effectiveness of this approach. **Aims:** The review aimed to summarize trial-based clinical and cost-effectiveness data on transdiagnostic CBT for anxiety and depression. **Method:** A systematic review of electronic databases, including peer-reviewed and grey literature sources, was conducted ($n = 1167$ unique citations). **Results:** Eight trials were eligible for inclusion in the review. There was evidence of an effect for transdiagnostic CBT when compared to a control condition. There were no differences between transdiagnostic CBT and active treatments in two studies. We found no evidence of cost-effectiveness data. **Conclusions:** Quality assessment of the primary studies indicated a number of methodological concerns that may serve to inflate the observed effects of transdiagnostic approaches. Although there are positive signs of the value of transdiagnostic CBT, there is as yet insufficient evidence to recommend its use in place of disorder-specific CBT.

Keywords: Transdiagnostic, cognitive behaviour therapy, systematic review, meta-analysis, methodological quality, evidence-base

Introduction

Depression and anxiety are highly prevalent (Kessler, Chiu, Demler, Merikangas and Walters, 2005; McManus, Meltzer, Brugha, Bebbington and Jenkins, 2009), have substantial impacts on quality of life and functioning for the individual (Haslam, Atkinson, Brown and Haslam, 2005; Paul and Moser, 2009) and are associated with substantial economic costs (Das-Munshi

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et al., 2008; Health and Safety Executive, 2012). Cognitive behaviour therapy (CBT) is an effective treatment for a range of depressive (Butler, Chapman, Forman and Beck, 2006; Hofmann, Asnaani, Vonk, Sawyer and Fang, 2012) and anxiety conditions (Olatunji, Cisler and Deacon, 2010; Otte, 2011), but the vast majority of evidence for the effectiveness of this approach is based on highly differentiated treatment protocols for specific diagnoses (NICE, 2011). An alternative approach, termed transdiagnostic CBT (tCBT), aims to identify a small number of cognitive and behavioural processes that are common across a range of depressive and anxiety conditions. These core processes are then used to develop a single treatment that can be applied across a range of presentations.

Proponents of tCBT have put forward a number of potential advantages to this approach. These include the possibility of offering more effective, efficient treatment of co-morbid presentations (Borkovec, Abel and Newman, 1995), something that is common in depression and anxiety presentations (Kessler et al., 2005). Furthermore, tCBT may reduce the training needs of therapists (Schmidt et al., 2012). Since tCBT by definition should be effective for a variety of different presentations, formation of ideally sized groups for group-delivered CBT should be simplified (Norton and Philipp, 2008).

There are potential disadvantages to tCBT, not as widely discussed in the literature. Clinical effectiveness may be diluted compared to diagnosis-specific treatments, because treatments are designed to treat a wide variety of disorders (Craske et al., 2007). It is unclear whether tCBT treatment is as acceptable to clients as disorder-specific CBT. When delivered in groups with a mixture of presentations, it may be difficult for clients to empathize with and learn as much from each other compared to groups in which clients have similar presentations (McEvoy, Nathan and Norton, 2009).

Three previous reviews have examined the effectiveness of tCBT. The first, Norton and Philipp (2008), was limited to anxiety studies. Of the nine studies reviewed, two were randomized controlled trials (RCTs) (Erickson, Janeck and Tallman, 2007; Schmidt et al., 2012) and one used a quasi-randomized design (Norton and Hope, 2005); the remainder used uncontrolled designs. The review calculated a large overall within-group effect size of transdiagnostic anxiety treatments ($d = 1.29$, 95% CI 0.66 to 1.93), compared to a small within-group effect size for control conditions ($d = 0.14$, 95% CI -0.21 to 0.49). The authors concluded that tCBT had considerable clinical utility, the preliminary data supporting the efficacy of the interventions.

The second review, McEvoy et al. (2009), included 10 studies, with one RCT (Erickson et al., 2007). The same quasi-randomized study was included, cited as two separate studies (Norton, Hayes and Hope, 2004; Norton and Hope, 2005). The remainder were uncontrolled studies. No meta-analysis of results was performed but a narrative synthesis concluded that tCBT protocols were highly promising, although additional research was required.

The third review, Reinholt and Krogh (2014), included five RCTs (Erickson, Janeck and Tallman, 2007; Farchione et al., 2012; Norton and Barrera, 2012; Roy-Byrne et al., 2010; and Schmidt et al., 2012), the quasi-randomized Norton and Hope (2005) and six uncontrolled studies. They reported a moderate combined effect size for all studies (SMD = -0.681 , 95% CI -0.903 to -0.458) favouring tCBT. The authors were more cautious in their conclusions than the previous reviewers.

Although the reviews were broadly positive about the effectiveness of tCBT approaches, caution is needed before accepting these conclusions. The reviews identified only a small number of RCTs; the majority of studies were based on uncontrolled designs. The RCTs

all compared tCBT to non-active control conditions, with the exception of Norton and Barrera (2012). There were a number of methodological limitations of the reviews when evaluated against standard guidelines for the conduct of systematic reviews (Moher, Liberati, Tetzlaff, Altman and The PRISMA Group, 2009). There was limited description of search strategies, and two reviews were limited to peer-reviewed publications, which may lead to an overestimate of effects because of publication bias (Dwan et al., 2008; Song, Eastwood, Gilbody, Duley and Sutton, 2000). There was limited evaluation of the methodological quality of included studies. Two reviews were conducted by researchers involved in tCBT protocol development. There is evidence that researcher allegiance can lead to inflated effect estimates in RCTs of psychological treatments (Luborsky et al., 1999). The case for tCBT would be strengthened by an additional independent review of the current evidence base.

Method

We adhered to the Centre for Reviews and Dissemination (2009) guidelines in the conduct of the review and PRISMA guidelines (Moher et al., 2009) in the reporting of the review.

Search strategy

The following databases were searched to cover peer-review and grey literature sources: PsycINFO, Medline, Embase, Cochrane Library, ASSIA, Web of Knowledge, OAIster, Open Grey, Trip Database and ZETOC. Additional searches were conducted in NHS EED, HTA Database, CEA Registry and RePEc health economic databases to identify relevant cost-effectiveness data. Databases were searched from inception to June 2013, with no publication status or language restrictions imposed.

Reference lists of included studies were examined, reverse-citation searches of included studies were conducted and websites of researchers and study groups in the field of tCBT were accessed to identify additional studies.

Search terms

Search terms, including free text and thesauri terms, were developed for PsycINFO and adapted for other databases (Appendix A). Terms covered two broad constructs, CBT and transdiagnostic treatment, combined using the Boolean AND. Search terms for CBT were adapted, with permission, from a systematic review of low-intensity psychological interventions (Rodgers et al., 2012). Search terms designed to capture the “transdiagnostic” construct were derived from searches of books, studies and articles uncovered during scoping searches. Thesauri available within the Ovid SP database were used to further inform search terms related to CBT.

Study inclusion and exclusion criteria

A priori inclusion and exclusion criteria were developed around standard criteria.

Participants. Adults (aged 16 years or over). Participants at baseline met diagnostic criteria for an anxiety or depressive disorder established by gold standard structured clinical

interviews or scored above a clinical cut-off point on a standardized severity measure. To ensure treatment was transdiagnostic, participants within studies must not have had uniform diagnoses.

Intervention. The intervention had to be described as tCBT (or use related terms such as Unified Protocol, mixed-diagnosis CBT, broad-spectrum CBT)

Comparator. Any comparison condition, including control or other active treatments.

Outcomes. Depression, anxiety or generic psychological wellbeing measured as a severity score or a dichotomous outcome (e.g. depressed, not depressed) and health economic data.

Study design. Randomized controlled trials. Quasi-randomized and uncontrolled trials were excluded.

Selection of studies

Two reviewers (PA, PT) used a pre-piloted eligibility form to assess studies. Disagreements were resolved through consensus and, where necessary, discussion with a third reviewer (DMcM). Titles and abstracts were first examined, and full papers obtained for studies passing this initial sift. Full papers were then re-examined using the eligibility form to determine final inclusion.

Data extraction

Data were extracted to a pre-piloted data extraction form by the primary reviewer (PA) and checked by the secondary reviewer (PT). Extracted data included study name, year and type of publication, authors, study location and setting, design, study sample characteristics, inclusion and exclusion criteria, description of interventions and controls, follow-up length, outcomes reported and data necessary to calculate effect sizes (e.g. means, standard deviations, sample size).

Quality assessment

Methodological quality and sources of bias were assessed using the Cochrane risk of bias assessment tool (Higgins et al., 2011) and an additional quality tool specifically tailored to assess the quality of psychological RCTs (Yates, Morley, Eccleston and Williams, 2005).

Data synthesis

Standardized mean differences (SMD) with 95 percent confidence intervals using Hedges's adjusted g (Hedges, 1981) were calculated for anxiety, depression and general psychological wellbeing severity measures.

Pre-planned comparisons. Results were grouped first by intervention type (individual or group), second by comparator (control condition or active treatment) and finally by outcome measure (anxiety, depression, general psychological wellbeing). If two or more studies were similar in terms of the intervention, comparator and outcome type, a meta-analysis was

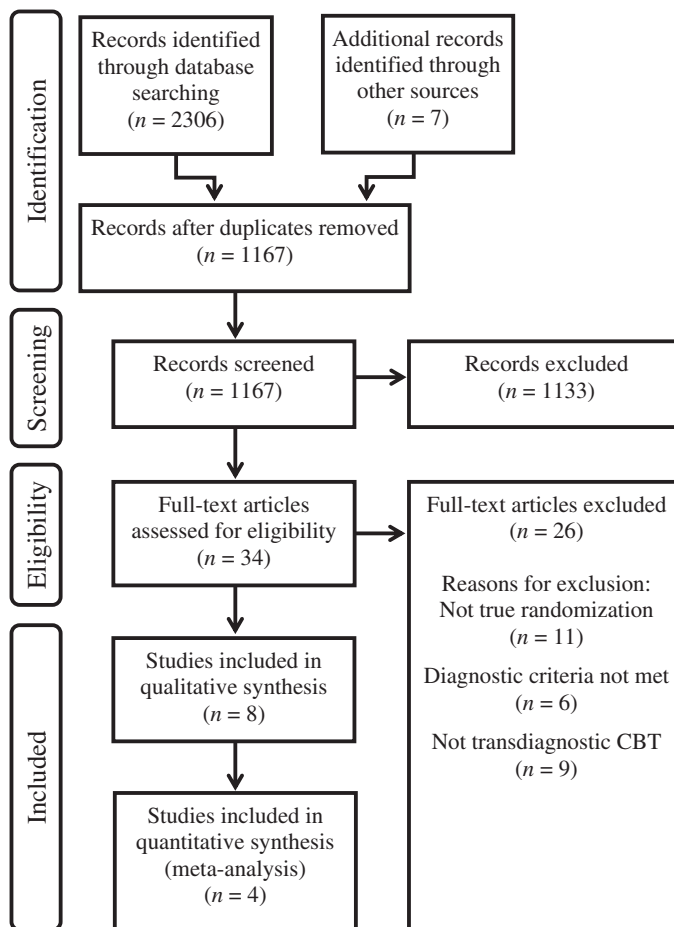


Figure 1. Search results and study selection flowchart

conducted. Heterogeneity was assessed using the I^2 statistic, with values over 50% taken to indicate substantial heterogeneity. Analyses were conducted in Review Manager 5 (Cochrane Collaboration, 2012).

Results

Electronic database searches identified 2306 citations. Seven additional unique records were identified through other sources. After removing duplicates, 1167 unique citations remained. Screening titles and abstracts excluded 1133 citations, leaving 34 full-text articles to be assessed. Of these, eight were judged eligible for inclusion in the review. Four studies were meta-analysed (see Figure 1).

Of 34 full-text articles assessed, 26 were excluded for the following reasons: 11 studies did not use randomization or used quasi-random methods of assigning participants to treatment;

nine studies were excluded for not using recognizable tCBT treatment protocols; participants in six studies did not meet diagnostic inclusion criteria (Appendix B).

Description of included studies

Table 1 summarizes the descriptive characteristics of the eight studies that met inclusion criteria for the review (Erickson et al., 2007; Farchione et al., 2012; Johnston, Titov, Andrews, Spence and Dear, 2011; Norton, 2012; Norton and Barrera, 2012; Schmidt et al., 2012; Titov, Andrews, Johnston, Robinson and Spence, 2010; Titov et al., 2011).

Table 2 summarizes the principal diagnosis of the total sample. Social phobia (32.3%), panic disorder (25.2%) and generalized anxiety disorder (29%) comprised the overwhelming majority of diagnoses. Depression was the principal diagnosis in only 5.2% of the entire sample.

Quality assessment of included studies

Table 3 summarizes the quality assessment of included studies using the Cochrane risk of bias tool. All studies were deemed at high risk of bias for blinding of participants and personnel, because this is typically inevitable in a trial of a psychological intervention. All studies were judged at high risk of bias in “other sources of bias” because of potential for research allegiance effects (treatment developers were the researchers evaluating their effectiveness). Unclear random sequence generation prompted an unknown risk of bias for this criterion in four studies (Erickson et al., 2007; Farchione et al., 2012; Norton, 2012; Norton and Barrera, 2012). Erickson et al. (2007) had an unknown risk of bias because of unclear information concerning blinding of assessors. This study was also assessed to be at high risk of bias due to selective reporting; two further were rated as having an unknown risk of bias on this quality item (Norton, 2012; Norton and Barrera, 2012).

Assessment of treatment quality within included studies

The Yates assessment tool (Yates et al., 2005) was used to assess quality of treatment administered in source studies. Items assessing description of treatment content and setting, description of treatment duration and manualization of treatment protocols were rated as present in all source studies. One study did not assess clinician adherence to the manual (Farchione et al., 2012). One study provided no information concerning therapist training (Erickson et al., 2007). Evidence of a lack of client engagement was identified in two studies (Norton, 2012; Norton and Barrera, 2012) (**Table 4**).

Clinical effectiveness

Clinical effectiveness results are grouped by type of comparator and mode of treatment delivery. Results are reported separately for each of the three main classes of primary outcome.

Table 1. Characteristics of included studies

Study	Setting and sample	Intervention/s	Comparator	Treatment focus/outcomes
Erickson et al. (2007)	Setting: Teaching hospitals, University training clinic, Canada Age (years): (Mean \pm SD) Intervention: 40.7 \pm 11.8 Comparator: 41.0 \pm 11.1 Overall: 40.9 \pm 11.4* Percent female: 63.8 Ethnicity: Not reported	Transdiagnostic CBT 11 X 120 minutes weekly groups Senior doctoral-level psychologist with senior graduate student <i>N</i> = 73 (47 at post-treatment)	Waitlist / delayed treatment <i>N</i> = 79 (41 at post-treatment) Note: Waitlist group began treatment 1 week after CBT groups completed treatment	Treatment focus: Anxiety Diagnosis: SCID Anxiety severity: BAI Depression severity: N/A Generic measure: N/A Measurement points: Baseline, post-treatment, 6-months post-treatment
Farchione et al. (2012)	Setting: University study clinic, USA Age (years): (Mean \pm SD) Intervention: 29.38 \pm 9.86 Comparator: 30.64 \pm 9.15 Overall: 29.75 \pm 9.66* Percent female: 59.5 Ethnicity: 94.6% Caucasian	Transdiagnostic CBT – Unified Protocol (UP) 18 X 60 minutes individual sessions Doctoral students, 2–4 years experience; licensed doctoral-level psychologist, 7 years experience <i>N</i> = 26 (22 at post-treatment)	Waitlist / delayed treatment <i>N</i> = 11 (10 at post-treatment) Note: Waitlist group began treatment 16 weeks after start of trial	Treatment focus: Anxiety Diagnosis: ADIS-IV Anxiety severity: HARS, BAI Depression severity: HRSD, BDI-II Generic measure: N/A Measurement points: Baseline, post-treatment, 6-months post-treatment
Johnston et al. (2011)	Setting: Internet, Australia Age (years): (Mean \pm SD) CL Group: 43.74 \pm 13.36 CO Group: 38.63 \pm 11.56 Comparator: 42.36 \pm 13.20 Overall: 41.62 \pm 12.83 Percent female: 58.8 Ethnicity: Not reported	1. Clinician assisted (CL) transdiagnostic iCBT (Anxiety Program) 8 units over 10 weeks Clinical psychologist <i>N</i> = 47 (42 at post-treatment) 2. Coach assisted (CO) transdiagnostic iCBT (Anxiety Program) 8 units over 10 weeks Registered psychologist <i>N</i> = 46 (39 at post-treatment)	Waitlist / delayed treatment <i>N</i> = 46 (41 at post-treatment) Note: Waitlist group began treatment immediately after iCBT groups completed treatment	Treatment focus: Anxiety Diagnosis: MINI Anxiety severity: GAD-7 Depression severity: PHQ-9 Generic measure: DASS-21 Measurement points: Baseline, post-treatment, 3-months post-treatment

Table 1. Continued

Study	Setting and sample	Intervention/s	Comparator	Treatment focus/outcomes
Norton (2012)	Setting: University anxiety clinic, USA Age (years): (Mean \pm SD) Overall: 32.98 \pm 10.73 Percent female: 62.1 Ethnicity: 58.6% Caucasian 21.8% Hispanic/Latino 9.2% African American 4.6% Asian American 5.7% other or mixed	Transdiagnostic CBT 12 x 120 minutes weekly groups Doctoral-level graduate students with experienced senior graduate co-therapists <i>N</i> = 65 (37 at post-treatment)	Relaxation 12 x 120 mins weekly groups Doctoral-level graduate students with experienced senior graduate co-therapists <i>N</i> = 22 (7 at post-treatment)	Treatment focus: Anxiety Diagnosis: ADIS-IV Anxiety severity: BAI Depression severity: N/A Generic measure: CGI-S Measurement points: Baseline, mid-treatment, post-treatment
Norton and Barrera (2012)	Setting: University anxiety clinic, USA Age (years): (Mean \pm SD) Overall: 31.46 \pm 8.93 Percent female: 50.0 Ethnicity: 54.3% Caucasian 23.9% Hispanic/Latino 10.9% African American 6.5% Asian American 4.3% Other or mixed	Transdiagnostic CBT 12 x 120 minutes weekly groups Doctoral-level graduate students with experienced senior graduate co-therapists <i>N</i> = 23 (16 at post-treatment) (57 total randomized, 12 declined treatment – allocation not stated)	Diagnosis-specific group CBT 12 x 120 mins weekly groups Doctoral-level graduate students with experienced senior graduate co-therapists <i>N</i> = 23 (12 at post-treatment) (See note in 'Intervention/s' column)	Treatment focus: Anxiety Diagnosis: ADIS-IV Anxiety severity: STAI Depression severity: BDI-II Generic measure: CGI-S Measurement points: Baseline, mid-treatment, post-treatment
Schmidt et al. (2012)	Setting: University outpatient clinic, USA Age (years): (Mean \pm SD) Intervention: 37.5 \pm 11.3 Comparator: 34.6 \pm 9.9 Overall: 36.3 \pm 10.7* Percent female: 71.9 Ethnicity: 83% Caucasian 10% African American 7% other	Transdiagnostic CBT – False Safety Behavior Elimination Therapy (F-SET) 10 x 120 minutes weekly groups Master's-level therapists (1 to 2 years clinical experience), experienced Ph.D. postdoctoral fellow <i>N</i> = 57 (53 at post-treatment)	Waitlist / delayed treatment <i>N</i> = 39 (39 at post-treatment) Note: Waitlist group began treatment immediately after CBT groups completed treatment	Treatment focus: Anxiety Diagnosis: SCID Anxiety severity: SPRAS Depression severity: BDI-II Generic measure: CGI-S Measurement points: Baseline, post-treatment, 6-months post-treatment (F-SET group only)

Table 1. Continued

Study	Setting and sample	Intervention/s	Comparator	Treatment focus/outcomes
Titov et al. (2010)	Setting: Internet, Australia Age (years): (Mean \pm <i>SD</i>) Intervention: 38.6 \pm 12.0 Comparator: 40.5 \pm 14.1 Overall: 39.5 \pm 13.0 Percent female: 67.9 Ethnicity: Not reported	Transdiagnostic iCBT (Anxiety Program) 6 units over 8 weeks Clinical psychologist via weekly telephone calls or instant messaging <i>N</i> = 42 (36 at post-treatment)	Waitlist / delayed treatment <i>N</i> = 44 (36 at post-treatment) Note: Waitlist group began treatment immediately after iCBT group completed treatment	Treatment focus: Anxiety Diagnosis: MINI Anxiety severity: GAD-7 Depression severity: PHQ-9 Generic measure: DASS-21 Measurement points: Baseline, post-treatment, 3-months post-treatment (treatment group only)
Titov et al. (2011)	Setting: Internet, Australia Age (years): (Mean \pm <i>SD</i>) Intervention: 44.8 \pm 14.9 Comparator: 42.9 \pm 14.5 Overall: 43.9 \pm 14.6 Percent female: 73.0 Ethnicity: Not reported	Transdiagnostic iCBT (Wellbeing Program) 8 units over 10 weeks Clinical psychologist via weekly telephone calls or instant messaging <i>N</i> = 39 (34 at post-treatment)	Waitlist / delayed treatment <i>N</i> = 38 (35 at post-treatment) Note: Waitlist group began treatment immediately after iCBT group completed treatment	Treatment focus: Anxiety or depression Diagnosis: MINI Anxiety severity: GAD-7 Depression severity: PHQ-9 Generic measure: DASS-21 Measurement points: Baseline, post-treatment, 3-months post-treatment (treatment group only)

Notes: * Calculated using pooled variance; ADIS-IV = Anxiety Disorders Interview Schedule for the DSM-IV; BAI = Beck Anxiety Inventory; BDI-II = Beck Depression Inventory (1996 revision); CBT = cognitive behavior therapy; CGI-S = Clinical Global Impressions - Severity scale; DASS-21 = Depression Anxiety Stress Scales - short-form version; F-SET = False Safety Behavior Elimination Therapy; GAD-7 = Generalized Anxiety Disorder 7-item scale; iCBT = internet CBT; MINI = Mini International Neuropsychiatric Interview Version 5.0.0; *N* = number of participants; N/A = not available; PHQ-9 = Patient Health Questionnaire - 9; SCID = Structured Clinical Interview for DSM-IV Axis I Disorders; *SD* = standard deviation; HARS = Hamilton Anxiety Rating Scale; HRSD = Hamilton Rating Scale for Depression; SPRAS = Sheehan Patient-Rated Anxiety Scale; STAI = State-Trait Anxiety Inventory

Table 2. Principal diagnosis of included participants

Principal diagnosis:	<i>N</i>	%
Social phobia	226	30.9
Panic disorder, with or without agoraphobia	177	24.2
Generalized anxiety disorder	203	27.7
Posttraumatic stress disorder	17	2.3
Obsessive-compulsive disorder	25	3.4
Specific phobia	8	1.1
Anxiety disorder not otherwise specified	4	0.5
Social phobia and anxiety NOS	1	0.1
Generalized anxiety disorder and social phobia	1	0.1
Obsessive-compulsive disorder and panic disorder	1	0.1
Major depressive disorder	38	5.2
Not reported	31	4.2
Total	732	100

Table 3. Cochrane risk of bias assessment tool summary

	Random sequence generation	Allocation conceal- ment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	Other bias
Erickson 2007	?	?	—	?	—	—	—
Farchione 2012	?	?	—	+	+	+	—
Johnston 2011	+	+	—	+	+	+	—
Norton 2012a	?	?	—	+	—	?	—
Norton 2012b	?	?	—	+	—	?	—
Schmidt 2012	+	+	—	—	+	+	—
Titov 2010	+	+	—	+	+	+	—
Titov 2011	+	+	—	+	+	+	—

Notes: + low risk of bias; — high risk of bias; ? unknown risk of bias

Table 4. Yates et al. (2005) treatment quality assessment tool

	Treatment content / setting	Treatment duration	Manualization	Adherence to manual	Therapist training	Client en- gagement	Total score
Erickson 2007	2	1	2	1	1	1	8
Farchione 2012	2	1	2	0	2	1	8
Johnston 2011	2	1	2	1	2	1	9
Norton 2012a	2	1	2	1	2	0	8
Norton 2012b	2	1	2	1	2	0	8
Schmidt 2012	2	1	2	1	2	1	9
Titov 2010	2	1	2	1	2	1	9
Titov 2011	2	1	2	1	2	1	9

Notes: Maximum total score is 9; higher scores denote lower bias

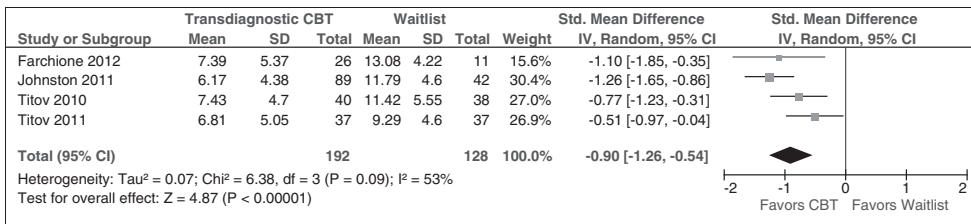


Figure 2. Individual transdiagnostic CBT vs. control conditions, anxiety measures

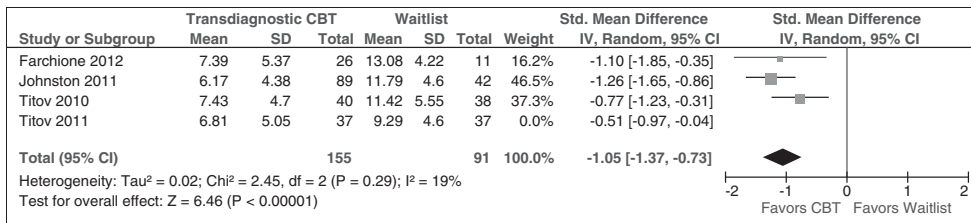


Figure 3. Individual transdiagnostic CBT vs. control conditions, anxiety measures, excluding Titov et al. (2011)

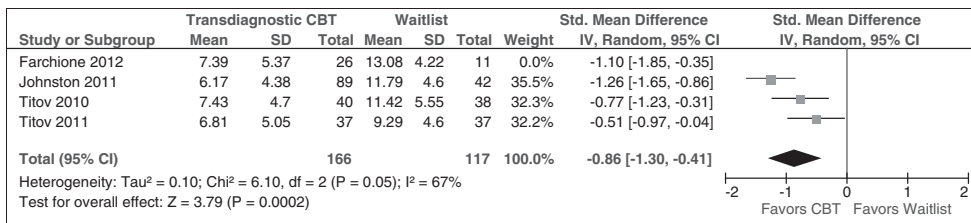


Figure 4. Individual transdiagnostic CBT vs. control conditions, anxiety measures, excluding Farchione et al. (2012)

Individual tCBT versus control conditions

Anxiety severity measures. Four studies provided posttreatment data from anxiety scales for individual tCBT versus waitlist control conditions (Farchione et al., 2012; Johnston et al., 2011; Titov et al., 2010, 2011) (see Figure 2). Farchione et al. (2012) used the Hamilton Anxiety Rating Scale (M. Hamilton, 1959) while the remaining studies utilized GAD-7 (Spitzer, Kroenke, Williams and Löwe, 2006). The data were re-analysed excluding Titov et al. (2011), a potential outlier (see Figure 3). To assess any difference between internet versus face to face treatment we excluded the single face to face study, Farchione et al. (2012) (see Figure 4).

Depression severity measures. The same four studies provided posttreatment data from depression scales (Figure 5). Farchione et al. (2012) utilized the Hamilton Rating Scale for

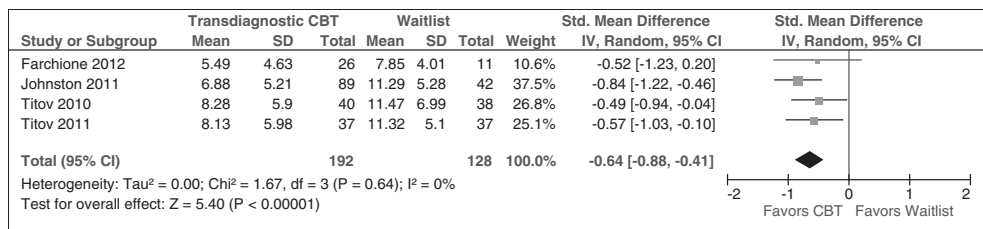


Figure 5. Individual transdiagnostic CBT vs. control conditions, depression measures

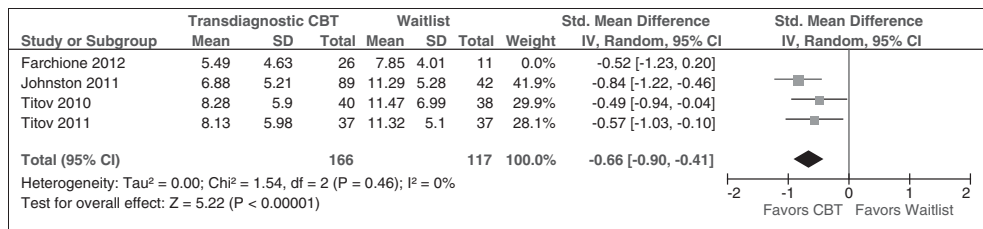


Figure 6. Individual transdiagnostic CBT vs. control conditions, depression measures, excluding Farchione et al. (2012)

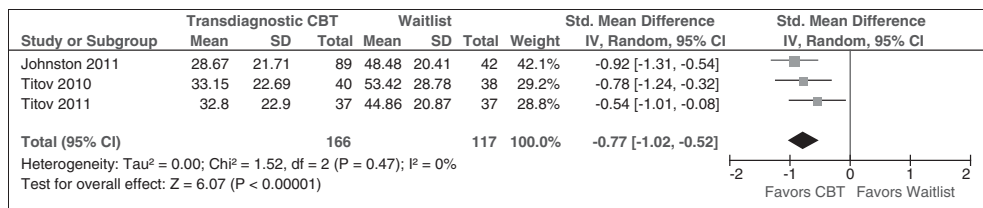


Figure 7. Individual transdiagnostic CBT vs. control conditions, generic measures

Depression (Hamilton, 1960) while the remaining studies used the PHQ-9 (Kroenke, Spitzer and Williams, 2001). For comparison, Farchione et al. (2012) was again excluded (Figure 6).

Generic severity measures. Three studies provided posttreatment data from generic scales for mental health (Johnston et al., 2011; Titov et al., 2010, 2011) (see Figure 7). Each used the DASS-21 (Lovibond and Lovibond, 1995).

Group tCBT versus control conditions

Anxiety severity measures. Two studies provided posttreatment anxiety data for group tCBT versus a control condition (Erickson et al., 2007; Schmidt et al., 2012). Erickson et al. (2007) used the BAI (Beck and Steer, 1990) while Schmidt et al. (2012) used the SPRAS (Sheehan, 1983). Results are not meta-analysed because of substantial heterogeneity ($I^2=80\%$, $p = 0.03$). Individual effect sizes are summarized in Figure 8.

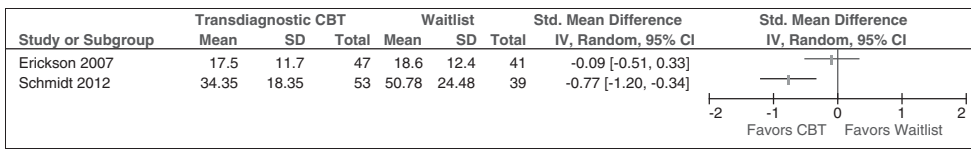


Figure 8. Group transdiagnostic CBT vs. control conditions, anxiety measures

Depression severity measures. Only Schmidt et al. (2012) provided posttreatment depression-specific severity data, using the BDI-II (Beck, Steer and Brown, 1996). The SMD was -0.38 , favouring tCBT (95% CI -0.80 to 0.04).

Generic severity measures. Schmidt et al. (2012) alone provided posttreatment generic mental health severity data. They used the CGI (Guy, 1976). The SMD was -0.99 , favouring tCBT (95% CI -1.43 to -0.55).

Individual tCBT versus other active treatments. No studies compared individual tCBT to another active treatment.

Group tCBT versus other active treatments.

Anxiety severity measures. Two studies provided posttreatment data from anxiety scales for group tCBT versus active treatment (Norton, 2012; Norton and Barrera, 2012). Norton (2012) used the BAI while Norton and Barrera (2012) used the STAI (Spielberger, Gorsuch, Lushene, Vagg and Jacobs, 1983). The studies were not meta-analysed because treatments, relaxation and disorder-specific CBT, were not considered similar enough that combining them would be meaningful. For Norton (2012) the SMD was -0.24 (95% CI -0.73 to 0.24), a non-significant difference favouring group tCBT over relaxation. The SMD for Norton and Barrera (2012) was 0.06 (95% CI -0.51 to 0.64), a non-significant difference favouring diagnosis-specific group CBT over group tCBT.

Depression severity measures. Norton and Barrera (2012) provided posttreatment depression-specific severity data using the BDI-II. The SMD was -0.25 (95% CI -0.83 to 0.33).

Generic severity measures. Both Norton (2012) and Norton and Barrera (2012) provided posttreatment generic mental health severity using the severity scale of the CGI (CGI-S). The SMD for Norton (2012) was -0.24 (95% CI -1.56 to 1.08). The SMD for Norton and Barrera (2012) was -0.22 (95% CI -1.35 to 0.92).

Cost-effectiveness

There were no studies identified that examined the cost-effectiveness of tCBT.

Discussion

The aim of the review was to assess the effectiveness of tCBT as evaluated in RCTs for depression and anxiety in adults. We identified eight studies, the majority of which were small

(total $N = 732$). One RCT included in the Reinholt and Krogh (2014) review was excluded because the intervention was a tailored CBT treatment rather than a single transdiagnostic protocol (Roy-Byrne et al., 2010). Four studies were of individual tCBT versus control conditions. These found evidence of significant effects in the moderate to large range for the outcomes of anxiety, depression and measures of generic mental health symptomatology. Two studies compared group tCBT with control conditions. Of the two studies, Schmidt et al. (2012) found some evidence of the effectiveness of tCBT, with significant effects ranging from small to large, though the effect reported for anxiety in Erickson et al. (2007) was non-significant. Only two studies compared tCBT to other active treatments, both of which used a group format of delivery. A meta-analysis was not conducted because of differences in the active treatment conditions. There was no indication of significant differences between tCBT and the other active treatment conditions. We found no data on the cost-effectiveness of tCBT treatment.

Limitations

These results must be considered in the light of both the limitations of the current review method and the primary studies themselves. Although we developed a systematic review protocol at an early stage of the review, we did not publish this on a database such as PROSPERO. Alternative definitions of transdiagnostic CBT, such as that offered by McEvoy et al. (2009), may be preferable to the operational definition we used because of the greater level of specificity offered.

Our review identified only eight RCTs involving tCBT. Although we made efforts to search grey literature, it cannot be ruled out that unpublished trials were missed, especially if descriptive terms used for treatments differed greatly from that found in scoping searches for this review. We found too few studies to formally assess the possibility of publication bias.

Allocation concealment is considered a key methodological standard of RCTs because there is evidence that absence of allocation concealment is associated with increased effect sizes (Schulz and Grimes, 2002; Wood et al., 2008). Four studies had unclear risk of bias for this item on the Cochrane risk of bias tool (Erickson et al., 2007; Farchione et al., 2012; Norton, 2012; Norton and Barrera, 2012). It is possible that estimates of effectiveness are overestimated in these studies. All studies were conducted by researchers who developed the transdiagnostic treatment protocols, a risk for researcher allegiance effects (Munder, Brüttsch, Leonhart, Gerger and Barth, 2013). This may also be associated with inflated effect sizes. Three studies were rated as either unclear or high risk of bias for selective reporting of outcome data (Erickson et al., 2007; Norton, 2012; Norton and Barrera, 2012). This form of bias typically inflates treatment effects, because results that are not positive may be less likely to be reported. Of concern was the absence of clear statements regarding primary outcome measures. This is a particular concern for the evaluation of transdiagnostic treatment, because it may not be clear what the most relevant outcome measure should be.

In summary, there are a number of methodological limitations of the primary studies, each of which may artificially increase observed effect sizes. This places an important caveat around the generally positive findings. Additional caveats include the small number of trials identified. Studies comparing tCBT to an active comparator were particularly scarce. The review found no transdiagnostic treatment cost-effectiveness evidence.

Research implications

The limitations of the primary studies suggest a number of implications for future research. First, future RCTs should adhere to accepted methodological standards for RCTs to minimize the possibility of bias. Adherence to the CONSORT statement in trial reporting would substantially improve this situation (Schulz, Altman and Moher, 2010). Researchers should publish trial protocols in which all proposed outcomes are stated and primary outcomes identified a priori. There is as yet an absence of independent evaluation of transdiagnostic treatments; trials to date have been conducted by researchers who developed the transdiagnostic protocols and are therefore at risk of researcher allegiance effects. Future research teams should consist of, in the words of Leykin and DeRubeis (2009), researchers “who possess complementary areas of expertise, and correspondingly opposite allegiances.”

While a number of studies provided follow-up data beyond the end of treatment it was not possible to calculate between-group effect sizes because, at the end of the treatment phase, control condition participants were immediately offered treatment. There is substantial evidence that disorder-specific CBT has an effect that continues beyond the end of treatment (Hollon, Stewart and Strunk, 2006; Steinert, Hofmann, Kruse and Leichsenring, 2014). Future trials should seek to use designs in which the ability of tCBT to reduce relapse relative to other conditions is examined. Future studies comparing tCBT to disorder-specific treatments should follow accepted standards for the design and analysis of non-inferiority RCTs (Fleming, Odem-Davis, Rothmann and Shen, 2011; Piaggio et al., 2012).

There are surprisingly few RCTs of transdiagnostic approaches covering both depression and anxiety presentations. There may be value in future studies examining the effectiveness of treatments designed for both anxiety and depressive presentations, particularly given the high degree of co-morbidity between these.

Future studies should incorporate concurrent economic evaluations, as this has not yet been formally evaluated. There would be value in adding qualitative components into future trials to establish the acceptability of tCBT interventions for both clinicians and clients.

Conclusions

The evidence base for tCBT as applied to anxiety and depression is at an early stage of development. While there are encouraging signs that the approach may be effective, it is important to consider the methodological limitations of the primary studies, many of which may serve to artificially inflate the observed effect of the intervention. There is very limited evidence on the comparative effectiveness of disorder-specific and transdiagnostic CBT approaches and an absence of cost-effectiveness evidence. Despite the encouraging signs, there is as yet insufficient evidence to recommend the use of tCBT in place of disorder-specific CBT approaches.

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Supplementary materials

To view supplementary material for this article, please visit
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References

- Beck, A. T. and Steer, R. A.** (1990). *The Beck Anxiety Inventory Manual*. San Antonio, TX: Psychological Corporation.
- Beck, A. T., Steer, R. A. and Brown, G. K.** (1996). *Manual for the Beck Depression Inventory-II*. San Antonio, TX: Psychological Corporation.
- Borkovec, T. D., Abel, J. L. and Newman, H.** (1995). Effects of psychotherapy on comorbid conditions in generalized anxiety disorder. *Journal of Consulting and Clinical Psychology*, 63, 479–83.
- Butler, A. C., Chapman, J. E., Forman, E. M. and Beck, A. T.** (2006). The empirical status of cognitive-behavioral therapy: a review of meta-analyses. *Clinical Psychology Review*, 26, 17–31.
- Centre for Reviews and Dissemination** (2009). *Systematic Reviews: CRD's guidance for undertaking reviews in health care*. York: Centre for Reviews and Dissemination, University of York.
- Cochrane Collaboration** (2012). *Review Manager (RevMan) [computer program]. Version 5.2*. Copenhagen: The Nordic Cochrane Centre.
- Craske, M. G., Farchione, T. J., Allen, L. B., Barrios, V., Stoyanova, M. and Rose, R.** (2007). Cognitive behavioral therapy for panic disorder and comorbidity: more of the same or less of more? *Behaviour Research and Therapy*, 45, 1095–1109.
- Das-Munshi, J., Goldberg, D., Bebbington, P. E., Bhugra, D. K., Brugha, T. S., Dewey, M. E., et al.** (2008). Public health significance of mixed anxiety and depression: beyond current classification. *British Journal of Psychiatry*, 192, 171–77.
- Dwan, K., Altman, D. G., Arnaiz, J. A., Bloom, J., Chan, A.-W., Cronin, E., et al.** (2008). Systematic review of the empirical evidence of study publication bias and outcome reporting bias. *PLoS ONE*, 3, e3081.
- Erickson, D. H., Janeck, A. S. and Tallman, K.** (2007). A cognitive-behavioral group for patients with various anxiety disorders. *Psychiatric Services*, 58, 1205–1211.
- Farchione, T. J., Fairholme, C. P., Ellard, K. K., Boisseau, C. L., Thompson-Hollands, J., Carl, J. R., et al.** (2012). Unified protocol for transdiagnostic treatment of emotional disorders: a randomized controlled trial. *Behavior Therapy*, 43, 666–678.
- Fleming, T. R., Odem-Davis, K., Rothmann, M. D. and Shen, Y. L.** (2011). Some essential considerations in the design and conduct of non-inferiority trials. *Clinical Trials*, 8, 432–439.
- Guy, W.** (1976). *ECDEU Assessment Manual for Psychopharmacology*. Rockville, MD: U.S. Department of Health, Education, and Welfare.
- Hamilton, M.** (1959). The assessment of anxiety states by rating. *British Journal of Medical Psychology*, 32, 50–55.
- Hamilton, M.** (1960). A rating scale for depression. *Journal of Neurology, Neurosurgery and Psychiatry*, 23, 56–62.
- Haslam, C., Atkinson, S., Brown, S. S. and Haslam, R. A.** (2005). Anxiety and depression in the workplace: effects on the individual and organisation (a focus group investigation). *Journal of Affective Disorders*, 88, 209–215.
- Health and Safety Executive** (2012). *Health and Safety Executive Annual Statistics Report 2011/12*. London: Health and Safety Executive (HSE).
- Hedges, L. V.** (1981). Distribution theory for Glass's estimator of effect size and related estimators. *Journal of Educational and Behavioral Statistics*, 6, 107–128.

- Higgins, J. P. T., Altman, D. G., Gøtzsche, P. C., Jüni, P., Moher, D., Oxman, A. D., et al. (2011). The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. *BMJ*, 343, 1–9.
- Hofmann, S. G., Asnaani, A., Vonk, I. J. J., Sawyer, A. T. and Fang, A. (2012). The efficacy of cognitive behavioral therapy: a review of meta-analyses. *Cognitive Therapy and Research*, 36, 427–440.
- Hollon, S. D., Stewart, M. O. and Strunk, D. (2006). Enduring effects for cognitive behavior therapy in the treatment of depression and anxiety. *Annual Review of Psychology*, 57, 285–315.
- Johnston, L., Titov, N., Andrews, G., Spence, J. and Dear, B. F. (2011). A RCT of a transdiagnostic internet-delivered treatment for three anxiety disorders: examination of support roles and disorder-specific outcomes. *PLoS ONE*, 6, e28079.
- Kessler, R. C., Chiu, W. T., Demler, O., Merikangas, K. R. and Walters, E. E. (2005). Prevalence, severity, and comorbidity of 12-month DSM-IV disorders in the National Comorbidity Survey Replication (NCS-R). *Archives of General Psychiatry*, 62, 617–627.
- Kroenke, K., Spitzer, R. L. and Williams, J. B. (2001). The PHQ-9: Validity of a brief depression severity measure. *Journal of General Internal Medicine*, 16, 606–613.
- Leykin, Y. and DeRubeis, R. J. (2009). Allegiance in psychotherapy outcome research: separating association from bias. *Clinical Psychology: Science and Practice*, 16, 54–65.
- Lovibond, S. H. and Lovibond, P. F. (1995). *Manual for the Depression Anxiety Stress Scales* (2nd ed.). Sydney, Australia: Psychology Foundation.
- Luborsky, L., Diguier, L., Seligman, D. A., Rosenthal, R., Krause, E. D., Johnson, S., et al. (1999). The researcher's own therapy allegiances: a “wild card” in comparisons of treatment efficacy. *Clinical Psychology: Science and Practice*, 6, 95–106.
- McEvoy, P. M., Nathan, P. and Norton, P. J. (2009). Efficacy of transdiagnostic treatments: a review of published outcome studies and future research directions. *Journal of Cognitive Psychotherapy*, 23, 20–33.
- McManus, S., Meltzer, H., Brugha, T., Bebbington, P. and Jenkins, R. (2009). *Adult Psychiatric Morbidity in England, 2007: results of a household survey*. Leeds: The NHS Information Centre for Health and Social Care.
- Moher, D., Liberati, A., Tetzlaff, J., Altman, D. G. and The PRISMA Group (2009). Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. *Annals of Internal Medicine*, 151, 264–269.
- Munder, T., Brüttsch, O., Leonhart, R., Gerger, H. and Barth, J. (2013). Researcher allegiance in psychotherapy outcome research: an overview of reviews. *Clinical Psychology Review*, 33, 501–511.
- NICE (2011). *Common Mental Health Disorders: identification and pathways to care*. Leicester and London: The British Psychological Society and The Royal College of Psychiatrists.
- Norton, P. J. (2012). A randomized clinical trial of transdiagnostic cognitive-behavioral treatments for anxiety disorder by comparison to relaxation training. *Behavior Therapy*, 43, 506–517.
- Norton, P. J. and Barrera, T. L. (2012). Transdiagnostic versus diagnosis-specific CBT for anxiety disorders: a preliminary randomized controlled noninferiority trial. *Depression and Anxiety*, 29, 874–882.
- Norton, P. J., Hayes, S. A. and Hope, D. A. (2004). Effects of a transdiagnostic group treatment for anxiety on secondary depression. *Depression and Anxiety*, 20, 198–202.
- Norton, P. J. and Hope, D. A. (2005). Preliminary evaluation of a broad-spectrum cognitive-behavioral group therapy for anxiety. *Journal of Behavior Therapy and Experimental Psychiatry*, 36, 79–97.
- Norton, P. J. and Philipp, L. M. (2008). Transdiagnostic approaches to the treatment of anxiety disorders: a quantitative review. *Psychotherapy: Theory, Research, Practice, Training*, 45, 214–226.
- Olatunji, B. O., Cisler, J. M. and Deacon, B. J. (2010). Efficacy of cognitive behavioral therapy for anxiety disorders: a review of meta-analytic findings. *Psychiatric Clinics of North America*, 33, 557–577.

- Otte, C. (2011). Cognitive behavioral therapy in anxiety disorders: current state of the evidence. *Dialogues in Clinical Neuroscience*, 13, 413–421.
- Paul, K. I. and Moser, K. (2009). Unemployment impairs mental health: meta-analyses. *Journal of Vocational Behavior*, 74, 264–282.
- Piaggio, G., Elbourne, D. R., Pocock, S. J., Evans, S. J., Altman, D. G. and CONSORT Group (2012). Reporting of noninferiority and equivalence randomized trials: extension of the CONSORT 2010 statement. *JAMA*, 308, 2594–2604.
- Reinholt, N. and Krogh, J. (2014). Efficacy of transdiagnostic cognitive behaviour therapy for anxiety disorders: a systematic review and meta-analysis of published outcome studies. *Cognitive Behaviour Therapy*, 43, 171–184.
- Rodgers, M., Asaria, M., Walker, S., McMillan, D., Lucock, M., Harden, M., et al. (2012). The clinical effectiveness and cost-effectiveness of low-intensity psychological interventions for the secondary prevention of relapse after depression: a systematic review. *Health Technology Assessment*, 16, 1–130.
- Roy-Byrne, P., Craske, M. G., Sullivan, G., Rose, R. D., Edlund, M. J., Lang, A. J., et al. (2010). Delivery of evidence-based treatment for multiple anxiety disorders in primary care: a randomized controlled trial. *JAMA*, 303(19), 1921–1928.
- Schmidt, N. B., Buckner, J. D., Pusser, A., Woolaway-Bickel, K., Preston, J. L. and Norr, A. (2012). Randomized controlled trial of false safety behavior elimination therapy: a unified cognitive behavioral treatment for anxiety psychopathology. *Behavior Therapy*, 43, 518–32.
- Schulz, K. F., Altman, D. G. and Moher, D. (2010). CONSORT 2010 statement: updated guidelines for reporting parallel group randomised trials. *BMJ*, 340, 698–702.
- Schulz, K. F. and Grimes, D. A. (2002). Allocation concealment in randomised trials: defending against deciphering. *The Lancet*, 359, 614–618.
- Sheehan, D. V. (1983). *The Anxiety Disease*. New York: Scribner.
- Song, F., Eastwood, A. J., Gilbody, S., Duley, L. and Sutton, A. J. (2000). Publication and related biases. *Health Technology Assessment*, 4, 1–115.
- Spielberger, C. D., Gorsuch, R. L., Lushene, R., Vagg, P. R. and Jacobs, G. A. (1983). *Manual for the State-Trait Anxiety Inventory*. Palo Alto, CA: Consulting Psychologists Press.
- Spitzer, R. L., Kroenke, K., Williams, J. B. and Löwe, B. (2006). A brief measure for assessing generalized anxiety disorder: the GAD-7. *Archives of Internal Medicine*, 166, 1092–1097.
- Steinert, C., Hofmann, M., Kruse, J. and Leichsenring, F. (2014). Relapse rates after psychotherapy for depression - stable long-term effects? A meta-analysis. *Journal of Affective Disorders*, 168, 107–118.
- Titov, N., Andrews, G., Johnston, L., Robinson, E. and Spence, J. (2010). Transdiagnostic internet treatment for anxiety disorders: a randomized controlled trial. *Behaviour Research and Therapy*, 48, 890–899.
- Titov, N., Dear, B. F., Schwencke, G., Andrews, G., Johnston, L., Craske, M. G., et al. (2011). Transdiagnostic internet treatment for anxiety and depression: a randomised controlled trial. *Behaviour Research and Therapy*, 49, 441–452.
- Wood, L., Egger, M., Gluud, L. L., Schulz, K. F., Jüni, P., Altman, D. G., et al. (2008). Empirical evidence of bias in treatment effect estimates in controlled trials with different interventions and outcomes: meta-epidemiological study. *BMJ*, 336, 601–605.
- Yates, S. L., Morley, S., Eccleston, C. and Williams, A. C. de C. (2005). A scale for rating the quality of psychological trials for pain. *Pain*, 117, 314–325.